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# MEDICAL NEWS LETTER

Editor - Captain L. B. Marshall, MC, USN (RET)

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### Graduate Training in Navy Hospitals

Applications for assignment to residency training duty are desired from Regular medical officers and those Reserve medical officers who have completed their obligated service under the Universal Military Training and Service Act, as amended. The following chart lists those Navy hospitals which currently have vacancies, and the specialties in which these vacancies exist:

	Bethesda, Md.	Chelsea, Mass.	Oakland, Calif.	Philadelphia, Pa.	Portsmouth, Va.	San Diego, Calif.	St. Albans, N. Y.
Anesthesia	x	x					
General Practice		x		x	x		
Internal Medicine		x			x	x	
Neurology	x		x				
Orthopedics	x	x					
Otolaryngology			x				
Pathology	x		x	x	x		
Pediatrics			x				
Psychiatry	x		x	x			
Radiology	x	x	x			x	
Surgery				x	x	x	
Urology					x		

Letters of application should be forwarded via official channels to the Chief of the Bureau of Medicine and Surgery, and should include an obligated service agreement prepared in accordance with the provisions of BuMed Instruction 1520.7.

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### Notice

Due to critical shortage of medical officers, the Chief, Bureau of Medicine and Surgery, has recommended, and the Chief of Naval Personnel has concurred, that Reserve medical officers now on active duty who desire to submit requests for extension of their active duty for a period of three months or more will be given favorable consideration.



### Policy

The U. S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be nor susceptible to use by any officer as a substitute for any item or article in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

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### New Director, Armed Forces Institute of Pathology

Captain William M. Silliphant, MC USN, has been appointed Director, Armed Forces Institute of Pathology, succeeding Brigadier General Elbert DeCoursey, MC USA, whose tour of duty ended on 1 August 1955. The nomination was made by the Board of Governors of the Armed Forces Institute of Pathology, composed of The Surgeons General of the Army, Navy, and Air Force, and was concurred in by the Secretary of Defense. This assignment is normally for four years and rotates in order among the Army, Navy, and Air Force. The Institute serves as the central laboratory of pathology for all the Armed Services, the Veterans Administration, and on a voluntary basis for the United States Public Health Service, the Atomic Energy Commission, and other Federal medical agencies.

Captain Silliphant received his Bachelor of Arts degree from the University of Southern California in 1926 and his medical degree from Stanford University Medical School in 1931. He was commissioned in the Medical Corps of the Navy in 1930 and interned at the U. S. Naval Hospital, Mare Island, California. At the termination of his first sea duty with the Pacific Fleet in 1933, he began postgraduate study in pathology at the Naval Medical School, Washington, D. C. Since then he has served as pathologist and Laboratory Officer at various Naval Hospitals, both in continental United States and overseas. From 1937-40, while stationed at the Naval Hospital, Pearl Harbor, he served concurrently as Pathologist to the Kapiolani Maternity Hospital in Honolulu, Hawaii. Assigned to the Naval Hospital, Canacao, Philippine Islands, one month before the Japanese began their conquest of those islands, he was captured and interned by the Japanese for 37 months. On the staff of Bilibid Prison Hospital

for Allied Prisoners of War, he served simultaneously as Ward Medical Officer, Sanitation Officer, and Laboratory Officer. Deprived of supplies and material with which to work, he claims the distinction of probably being the only pathologist ever to have run a laboratory without the aid of a microscope, or to have resorted to burying vaccines in the ground for their preservation in lieu of refrigeration.

Returning to this country after the liberation of the Philippines in the winter of 1945, he served successively as Chief of Medicine and Pathologist at the U.S. Naval Hospital, Long Beach, California. In 1947, he was transferred to the Naval Medical School, National Naval Medical Center, Bethesda, Maryland, where for a period of five years he served as Director of Laboratories and Executive Officer as well as Consultant to Professional Division, Bureau of Medicine and Surgery. While in this position he served as an original member of the "Hawley Board" Subcommittee on the Army Institute of Pathology, which, following the recommendations of this subcommittee, became the present-day Armed Forces Institute of Pathology. He was also the Navy's representative on the "Hawley Board" subcommittee which recommended the integration of the Armed Forces Medical Library within the Armed Services. Since February 1952, he has been the Navy Deputy Director of the Armed Forces Institute of Pathology.

In the spring of 1953, Captain Silliphant volunteered as Pathologist on a Wound Ballistics Research Team, being sent to the Far East for survey studies on Korean Casualties with particular reference to the influence of body armor on war wounds. He was engaged in this study at the time of the Korean Armistice. Present at Freedom Village during Big Switch in August 1953, he was able to observe some of the effects of Communist internment on newly liberated POW's. Among those whom he met returning from enemy prison camps were two United States Marines who had formerly been POW's with him in World War II.

Captain Silliphant is a Diplomate of the American Board of Pathology and a Fellow of the American Medical Association, the American College of Physicians, the American Association of Pathologists and Bacteriologists, and the American Society of Clinical Pathologists. He is a member of the Phi Beta Pi Medical Fraternity. To medical literature, he has contributed articles on bronchogenic carcinoma, eosinophilic granuloma, wound ballistics, and comparative studies of the Kahn and Cardiolipin tests for syphilis. For distinguished service while a prisoner of war, the Secretary of the Navy issued him the Navy Letter of Commendation with Commendation Ribbon. He was also awarded the Army Distinguished Unit Badge, Philippine Defense 1941-1942; and from the Philippine Government, the ribbons of Philippine Defense, Philippine Liberation, and Philippine Independence.

Captain and Mrs. Silliphant make their home at 3811 Woodbine Street, Chevy Chase, Maryland. They have two daughters, Mary Ruth, who attends the University of North Carolina, and Elizabeth Ann, a Junior at the Bethesda-Chevy Chase High School, Bethesda, Maryland.



Naval Medical Research Institute  
National Naval Medical Center, Bethesda, Maryland

(The following information was abstracted from a report made by Captain W. E. Kellum, MC USN, Commanding Officer of the Institute, to the Surgeon General.)

The first components of NMRI were placed in commission in 1942, further rapid development of the Institute followed and a new wing and animal house were added almost immediately. A temporary building to house excellent diving and pressure chamber equipment and the battleship compartment followed. In due course, the shops and aviation medicine moved into a garage building. Small buildings for the cobalt irradiator, the human calorimeter and the maxitron were added. Construction of the west wing of the main building started 11 July 1955.

During the war years, the efforts of the Institute were directed largely to the solution of practical military problems. The organization was essentially a military one, the staff were all in uniform.

The end of the war brought reorganization problems. Most of the civilian scientists in uniform left the Service. The policies and plans which now guide the management of the Institute were evolved gradually over the succeeding years. The plans and policies are in part as follows: The Institute must limit its size, but the quality of the staff and the character of the work are to be of the best. Uniformed personnel are to be included in the staff with a view to maintaining close touch with the operational Navy. The need for civilian scientists of maturity and established stature in certain fields of science is recognized. The scientists should be free to work in basic science but should be available to bring their special abilities to bear on Navy problems. It follows that the disciplines represented should be basic to medical science. The staff should be able to support the work in field laboratories by consultation and collaboration. The staff and unusual facilities of the Institute should also be able to support clinical research in the Naval Hospital and in the Medical and Dental Schools. Finally, the consultative services of the staff should be available to the Bureau of Medicine and Surgery.

Progress toward these ideals was slow and tedious in the beginning. Particularly was this true in building a staff. Scientists needed to know what sort of an institute would take shape, what opportunities they would have to pursue their scientific interests, what quality of associates they would have. The Institute has attained a reputation in the scientific world which makes it possible to attract able men.

NMRI is not thought of as a large organization. However, a powerful research staff, that for excellence need be second to none, can be developed. A fair start in that direction has been made. It will be necessary to add a few scientists and, in time, a modest increase in supporting staff will be

needed. The establishment of four or five postdoctoral fellowships will do much to increase the effectiveness of the staff.

Steady increases in the amount of collaborative work with the Medical School and the Hospital is reported. A determined effort is being made to make the staff more useful in supporting the research programs in other naval medical research laboratories and to encourage interlaboratory collaboration. Outside the Navy, a great deal of collaborative work is in progress. This is most extensive with the National Institutes of Health. At the same time, close association with Johns Hopkins and with the local universities continues. Some of the staff are engaging in joint work with scientists in the other laboratories further away. There are collaborative studies with laboratories at Oxford and Cambridge. NMRI is the focal point for a broad scale study of the factors underlying human performance.

Captain Kellum briefly reviewed some of the research in progress as follows:

One of the most brilliant groups is working with Dr. Morales on the mechanism of muscle contraction. This group which includes Doctors Steiner, Botts, Blum, Hill, and Podolsky (who is spending a year with A. V. Hill in Cambridge) have characterized the myosin molecule and shown it to be a large spiral shaped molecule capable of contracting and extending. They have shown the part played in this reaction by the splitting of adenosinotriphosphate by the enzymatic action of myosin. With Dr. Kitzinger and the microcalorimeter, they have measured precisely for the first time the amount of energy released by this process. Their work, which has attracted international attention, is being continued. This is basic research of a sort that should give a better understanding of muscular work, of fatigue, and human performance.

The microcalorimeter has been developed by Doctors Benzinger and Kitzinger to a degree of perfection which permits the accurate measurement of fantastically small amounts of heat, .00009°C. At present, it is being used in collaboration with Dr. Calvin of the University of California and a group under Dr. Horecker at N.I.H., to measure the heat involved in one phase of the photosynthesis by which carbon dioxide is incorporated in the carbohydrate molecule.

The Tissue Bank is an example of joint effort of which all are proud. The basic studies were done at NMRI where a succession of young Reserve medical officers have kept the program going through the past six years. When the results warranted it, the work was passed to the Naval Medical School and the Hospital to be used in human surgery. The sterile autopsies at the Medical School and the use of the freeze-dried tissues in surgery are now known. This work continues on a collaborative basis. Just now, representatives of the Medical School and the Hospital are working in NMRI laboratories on methods of preserving corneal transplants. Studies of the



immunity response which causes heterologous grafts to be rejected by the host tissues are being pushed forward in collaboration with a group at California Institute of Technology. Dr. Losee of the dental group, in addition to brilliant new work on dental caries, is succeeding in efforts to make heterologous bone grafts acceptable to animal hosts. Some of the experimental surgery group are turning to fundamental studies of the physiology of hypothermia and have recently made important contributions to the literature of the subject.

Dr. Rosenfeld, in collaboration with the Worcester Foundation for Experimental Biology at Worcester, Mass., has developed perfusion techniques and applied them to studies of the physiology of the adrenal cortex. Among other achievements, he has developed an artificial fluid to be used in place of blood in their perfusion experiments. This technique, which is a significant contribution, eliminates several troublesome elements, such as blood cells, antigens, complex proteins, et cetera. Presently, the effects on the adrenal of exposure to radiation are being studied in calves with the cobalt irradiator.

Dr. Hurley reported the work he and Dr. Hardenbergh have done on the effects of frostbite and the importance of rapid rewarming after exposure to severe cold.

In submarine and diving medicine, Dr. Stein and his group are working on two basic problems of immediate importance to the Navy. Dr. Williams as collaborator in this work has found what appears to be rather specific pathology in the lungs of monkeys which have been kept for periods of 90 days or less in an atmosphere containing 4.5% of carbon dioxide. This is a tentative report at present. The other problem engaging this group is the matter of oxygen toxicity which has become a matter of vital importance in the Navy's underwater operations.

In the area of the effects of other physical forces, two major studies are in progress: the biological effects of exposure to high-powered radar and the effects of vibration applied to the body as a whole. It is too early to report results from either of these studies.

In the field of parasitology, malaria is still of concern. Dr. Huff and LCDR Weathersby have been doing some brilliant work with the study of malaria in tissue cultures. Dr. Terzian's work appears to indicate that the mosquito, herself, can be used as a means of testing and studying antimalarial drugs.

The study of schistosomiasis continues here under LCDR Lincicome.

NMRI has scored a brilliant success in the problem of filariasis. This disease in World War II cost the Navy loss of man-power to the equivalent of a battalion of Marines for four years and enough money to run NMRI for 25 years. Due to the work of LCDR Jachowski and the group from Johns Hopkins who worked with him such losses from this cause need never again be faced.

NMRI reports the successful preservation of human blood by freezing. Dr. Meryman, applying knowledge developed in two or three years of pure basic research, has succeeded in freezing and reconstituting blood. Using cells tagged with radioactive chromium, two transfusions have been accomplished with no more loss of red cells than occurs in a normal transfusion. The only substance added in the process is a small amount of dextrose. Much remains to be done before the process is a proven practical success, but the critical problems appear to have been solved.

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### Chelating Agents

A metal chelate is a special form of a complex or coordination compound. A coordination compound is one in which a metal ion and an organic molecule are bound together by a coordinate valence, a special type of binding wherein the organic portion (or donor) contributes both electrons necessary to form the bond. Inorganic atoms can also be donors so that entirely inorganic complexes also occur.

In a complex or coordinate type of structure, such as organic metal chelates, the metal loses its original characteristics as an ion. Thus, for example, Ca ion, in combining with citric acid forms a complex in which the characteristic effects of the Ca ion are no longer apparent, i. e., it will no longer be precipitated by alkaline phosphate or coagulate plasma, nor will it exert the typical effects on nerve and muscle. When a complexing agent combines with a metal ion so that two or more of the functional groups of the organic molecule attach to the metal ion and one or more rings are formed, the resulting compound is termed a chelate. Nearly all of the metals in the periodic system form complexes or chelates. In general, organic compounds which are likely to be chelating agents are those which contain N, O, or S attached to an active H.

The combination of a metal ion with an organic molecule in a chelate structure often confers new properties which are not apparent in the metal ion or organic moiety when each is considered alone. These are the means used to determine the formation of chelates. Among these changes are color (many dyes owe their color to chelate formation), electrical conductivity (as a rule conductivity drops as more and more chelate is formed in solution), changes in solubility, chemical reactions, magnetic susceptibility, and others. Of great interest are the situations in which chelate structure formation confers biological activity. Hemoglobin, catalase, carbonic anhydrase, various keto acid carboxylases, cytochromes, arginase, phosphatase, and phosphate-transferring enzymes--all are metal chelates or are postulated to exert their biochemical activity through the reversible formation of metal chelates or complexes.



In view of the powerful effects these materials naturally exert in the body, it is not surprising that attempts have been made to use synthetic chelating agents for various medical and investigative purposes. For many years, advantage has been taken of the solubility characteristics of chelates as means of introducing metals into the body as an attempt at therapy. Preparations for parenteral administration of Fe, Ca, Mg, Bi, Sb, and Au as the citrates, gluconates, salicylates, and thiomalates--to mention just a few--are chelates or complexes.

In recent years, considerable research has been carried on in which synthetic chelating agents have been used as competitors for metals in biological systems as a means for studying enzymes. Attempts have been made to remove metal ions from the body by the use of chelating agents.

B. A. L. is a chelating agent of considerable usefulness in pulling remaining metals from the body, in particular, Hg, As, and Bi. Not only does it deplete the body rapidly of the metal ion but it also alleviates the associated symptoms, a factor of importance not always seen in this type of therapy. It is not useful in Pb poisoning. The only radioactive material which currently constitutes a health hazard for which B. A. L. has been found efficacious is Po.

Among other chelating agents used for biological purposes are Na procatechol disulfonate and Schubert's aurintricarboxylic acid and salicylic acid. Sodium pyrocatechol disulfonate has been tried in the treatment of saturnism by Italian workers. In this laboratory, Ca EDTA is the compound with which the most work has been done, and in many respects it has proved to be almost ideal.

EDTA forms very stable chelates with most metal ions. It is most desirable that the agent form strong binding with the metal to be removed, and that this binding should exceed natural binding forces. The metal to be removed must have a higher stability constant than essential metals in order that the latter not be depleted. EDTA meets these demands.

There are several other requirements in order that a chelating agent may be useful for therapeutic purposes. It is essential that the metal chelate formed in the body be readily excreted, and for this to occur, it is highly desirable that water-soluble chelates be formed. In addition, it is important that the agent not be broken down in the body; the agent must not be toxic, that is, there should be a wide range between therapeutic dose levels and toxic dose levels.

Ca EDTA is a relatively non-toxic drug. Metabolic studies using C<sup>14</sup>-labeled material indicate that it passes through the body unchanged. It is excreted via the kidney by both glomerular filtration and tubular excretion. The turnover time from the blood is approximately one hour after intravenous administration and one and one-half hours after intramuscular injection. It quickly mixes with almost all of the body water except that it does not pass into the red cells and passes relatively slowly into the



spinal fluid compartment. It is poorly absorbed from the gastrointestinal tract.

Many cases of lead poisoning have been treated with EDTA by workers in various parts of the country. The most spectacular and favorable results have occurred in children with Pb encephalopathies, where the use of the drug produced very satisfactory alleviation of convulsions and coma. In adults, the use of the drug was followed by a manifold increase in Pb urinary excretion and, in a number of instances, by objective signs of increased well-being of the patient, i. e., decrease in coproporphyrins and stipple count, and alleviation of anemia.

EDTA appears to be of value in the treatment of Pu cases, particularly in the early time period. In view of the innocuousness of small doses of the drug and the importance of early treatment, it is felt that it would be sound practice to give the material as soon as exposure is suspected. No harm is done from giving the drug, and the time gain would be valuable. The diagnosis of exposure from the first 24-hour urine specimen will not be obscured by the procedure. (Foreman, H., Chelating Agents: Indust. Med., 24: 287-291, July 1955)

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#### Schema for Treatment in Tuberculosis

The advances of the last 10 years in the treatment of tuberculosis have revolutionized the management of this disease in all of its clinical forms. Each new development has followed on another so rapidly that it has been impossible to fully evaluate a method of treatment before it is displaced by some modification, or by a totally new treatment which looks better. It is small wonder, therefore, that, in this disease which has so many special characteristics, and for which the perfect treatment is not yet at hand, there should be now a period of uncertainty, confusion and disagreement.

This uncertainty pertains not only to the selection of specific drugs and the indications for various surgical procedures, but even to the place where patients should be treated (in hospitals or at home) and by whom they should be treated. One group may wish to issue statements urging that all tuberculous patients be treated in tuberculosis hospitals, while another may suggest that special tuberculosis hospitals are rapidly becoming obsolete. There is not even agreement on the trends of prevalence, in this country and abroad, and no one seems to know whether the disease is becoming more or less important.

One thing, at least, is known, Tuberculosis is still existent. Many patients with tuberculosis in one form or another appear in doctors' offices, in clinics, in hospitals, or are detected in surveys. They all require



medical management, and many require active treatment. Physicians cannot wait for the results of long-term follow-up studies now in progress, which may and probably will determine which of the currently available methods is the best in each type and variety of case. By the time these answers are forthcoming, more likely than not, there will be new developments which will cause the best of present methods to be outmoded.

Meanwhile, there is the necessity to be systematic, not only in the comparative study of different modes of treatment, but in thinking about treatment problems. It is not enough that such excellent comparative studies be made as those organized by the Veterans Administration, the U. S. Public Health Service, and Great Britain's Medical Research Council. Not all patients can or should be treated according to chance selection. Control studies of this type have many limitations. Moreover, they are justified only when expected differences in results are relatively small and undeterminable by less arbitrary methods of clinical evaluation.

The author believes that too much emphasis is often placed on mathematically significant differences when the basic observations are as subjective as, for instance, the roentgenographic evaluation of the progress of pulmonary tuberculosis under therapy. The very terms "better" and "worse" are incapable of precise definition in roentgenographic terms. When one comes to attaching great significance to 1-plus, 2-plus, or 3-plus "improvement," and attempts a determination of the "best" treatment on statistical analysis of such arbitrary data, one is building on a somewhat unstable foundation. Yet, sweeping recommendations have often been made on no firmer basis than this. Unfortunately, too great reliance on comparative regimen studies seems, sometimes, to discourage independence of thought and to permit outmoded treatments to persist overlong.

For example, many of the articles on the antimicrobial therapy of tuberculosis, published within the past year or two, still recommended streptomycin and PAS as the "therapy of choice" in pulmonary tuberculosis. This recommendation was made even though it was recognized explicitly or implicitly in these reports that, in the most serious forms such as miliary and meningeal tuberculosis, it is essential to include isoniazid, and that isoniazid is itself the most effective, the cheapest, and the least toxic antituberculosis drug available. Even while acknowledging these superior qualities of isoniazid, a great many experts insisted that it must never be used alone and that usually it should never be used in initial treatment.

Little consideration has been given, until recently, to the possibility that different forms of tuberculosis, or different types of pulmonary tuberculosis might be more satisfactorily treated by different drug regimens. On present evidence, it seems highly probable that the best management of tuberculosis will prove to be, not a single drug regimen which is optimal for all cases (as seems to have been the goal and the orientation of most

investigations up to the present time), but that different regimens will be found to best suit different forms and types of the disease. To determine such selective indications on a thoroughly scientific statistical basis, however, will require so much manipulation of groups and subgroups and so much time that it is not realistic to suspend action in this field until proof is at hand. The same may be said concerning the use of resectional surgery for various types of lesions, the use of pneumothorax or pneumoperitoneum, the duration and conditions of rest treatment, and decisions whether or not to insist on hospitalization. All or most of these questions should be systematically investigated, but it is unlikely that they all will be, or that unequivocal results will be obtained in time to greatly affect patterns of action which will inevitably evolve in the meanwhile.

Accordingly, the author believes that there is a great necessity at the present time to formulate a schema for the treatment of tuberculous disease; that this can be done now on a rational basis, taking advantage of the established facts and, when necessary, attempting to anticipate the strongest probability of the future. Such a formulation has been conspicuously absent from current discussions and is considered by the author to be, perhaps, a hazardous undertaking. The present situation, however, borders so nearly on chaos and the emphasis has been so predominantly on the disadvantages of practically every type of treatment, that he undertakes this self-imposed task without apology. It is presented for consideration and discussion, with no claim that it represents finality. It is nothing more than a crystalization of his own thought and practice of the past year or two. If, in some respects, the schema appears to conflict with current majority concepts, it is not because of any light-hearted fondness for "heresy." The belief that the present uncertainties and conflicts need to be resolved is accompanied by some sense of urgency. No attempt is made to go into details of dosage, which are well known, nor is there more than passing mention of drugs which are still entirely in the investigative stage and are as yet unapproved for prescription sale in the United States.

The author discusses the treatment of tuberculosis under the headings, Miliary and Meningeal Tuberculosis, Pulmonary Tuberculosis, and Extrapulmonary Tuberculosis. (Muschenheim, C., A Schema of Treatment in Tuberculosis: Am. Rev. Tuberc., 72: 1-3, July 1955)

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#### Autoerythrocyte Sensitization

It is generally known that some women bruise easily and develop ecchymoses, particularly in the lower extremities, without definite trauma. Studies of the blood clotting factors in such individuals have yielded normal or equivocal results. This vague hemorrhagic diathesis



has been called "purpura simplex" and described as consisting merely of easy bruising and bleeding into the skin and subcutaneous tissues. The occurrence is usually of minor annoyance to the subject and is otherwise of little significance.

In contrast, this report describes the occurrence in four women of an abnormal response to bruising, characterized by local pain, swelling, and extension of bleeding into adjacent areas, often to a serious extent. The histories and laboratory investigations suggest that, in these patients, there has occurred a sensitization against one of their own body tissues, namely red blood cells. The clinical histories of these four women are presented to describe this disorder. The methods and results of investigation are outlined to demonstrate the abnormal tissue response associated with sensitization to red blood cells.

Observations in this group indicate a tissue sensitivity to extravasated red blood cells. All had had trauma associated with bruising which preceded the onset of the painful ecchymotic lesions. The writers believe that the term "erythrocyte autosensitization" might be used to describe what occurred in these cases. Previous clinical observations have suggested that generalized dermal sensitivity could develop from chronic eczematoid lesions. Whitfield emphasized the concept of autosensitization for skin lesions.

The recurrent lesions observed in these patients may be confused with relapsing, febrile, nodular, non-suppurative panniculitis (Weber-Christian Disease). The onset of the lesions is associated with erythema and induration. In contrast to patients with panniculitis, none of the patients reported here have developed subcutaneous atrophy or nodules. Likewise, febrile reactions have been rare and associated only with a large extending ecchymotic area. As the ecchymosis disappeared, the skin became normal to palpation and appearance. Leukopenia was not observed.

Despite the frequent hematomas associated with trauma in hemophilia, painful ecchymoses, due to a possible sensitivity reaction, have not been reported. Likewise, in ecchymoses seen in many types of purpura, this response has not been described. Also, no case, similar to the four here described, has been seen in men.

No specific therapy is available for this form of purpura. Three of the four women have had a marked decrease of this abnormal response to bruising without explanation. Splenectomy was done in two patients. One patient had complete absence of the tissue sensitivity for a three-year period following splenectomy, only to have a recurrence which has persisted to a lesser degree until the present time. The other patient showed no improvement after surgery, but gradually lost the abnormal tissue response during the next 5 years and is now subjectively free of the painful bruising. However, the latter patient still shows an abnormal response to intradermal skin tests with packed red cells.



Four patients with purpura, who manifested an unusual response to bruising, were studied. This response was characterized by the development of an area of painful ecchymosis at the site of trauma, followed by progressive erythema and edema. This unusual tissue response was seen only in women. The various features of the cases suggested an autosensitization by the patients to their own blood.

Special studies, utilizing skin testing procedures, indicated an abnormal tissue response of sensitivity to red blood cells. The factor responsible was present in the red cell stroma and was not associated with the hemoglobin.

Clinical manifestations and possible therapy are discussed. This syndrome may represent another example of autosensitization such as has been speculated for lupus erythematosus, some forms of acquired hemolytic anemia, and of thrombocytopenic purpura, and for an increasing number of disease states. (Gardner, F. H., Diamond, L. K., Auto-erythrocyte Sensitization: Blood, X: 675-689, July 1955)

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#### Evaluation of Hypaque in Excretory Urography

The purpose of this article is to summarize in a preliminary report the results obtained in 300 patients following the use of hypaque as a contrast medium for intravenous urography. A comparison was made between the results already obtained following the use of diodrast.

The object of the study was (1) to determine the efficiency of hypaque as an intravenous medium, and the number and seriousness of the reactions associated with intravenous injection of the dye; (2) to correlate the results of the preliminary testing procedures with subsequent reactions; and (3) to determine the relative effectiveness of hypaque in delineating the urinary tract. The patients were selected at random. The preliminary precautionary measures, outlined by Robbins and associates, and Pendergrass, were utilized. In addition, an oxygen tank was maintained in the urologic rooms and the personnel of the departments were instructed in its use. Prior to the intravenous injection of the drug, the patient was specifically questioned as to whether a history of an allergy existed or whether there was a history of hay fever, asthma, eczema, or hives. In addition, queries were made concerning reactions following the administration of previous drugs. The patient was specifically questioned by both technician and physician, and in no case was an intravenous urogram undertaken by a technician alone. If the blood chemistry studies and the specific gravity did not warrant the study, it was rarely undertaken. If, in the survey of the patients, a history of allergy was elicited, preliminary testing by means of ocular, oral, dermal, or intravenous methods was undertaken.



One or more of the testing methods were utilized in all of these cases. A chart was devised for the testing of the hypaque so that recordings of the changes in the blood pressure, respiration, and subsequent laboratory findings could be made. The chart served as a reminder for the testing procedures to be followed in each patient.

The medium resembles urokon in its pattern of excretion, differing from diodrast in that the kidney visualization appeared more rapidly with hypaque. Sharper delineation with increased concentration of the dye was found with hypaque. The contrast produced by 50% hypaque produced densities simulating those when urographic media of 70% concentration are utilized. Approximately 85% of the urograms completed, following hypaque injection, were considered good or excellent in quality.

The drug is rapidly eliminated in an unchanged form. Hypaque, when tested in experimental animals, was extremely well tolerated in doses many times that of the probable clinical dose.

Exceedingly few reactions of any type were encountered in this study. One or more of the following signs were noted in 8 patients: nausea, vomiting, dizziness, and transient flushing. A total of 15 patients showed reactions even when minor vasomotor and psychogenic side effects were included. No true allergic signs were noted. The virtual absence of vein cramp was noteworthy. Only after a large segment of the patient population has been studied, can adequate conclusions be drawn. The comparative safety of hypaque might be indicated by the extremely low incidence of vasomotor reaction. Hypaque, thus far, has proved to be a satisfactory, effective, efficient, and safe means of delineating the urinary tract. (Lowman, R. M., et al., Preliminary Clinical Evaluation of Hypaque in Excretory Urography: Surg. Gynec. & Obst., 101: 1-8, July 1955)

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#### Single Aspiration Caffeine Test

In most patients, the diagnosis of duodenal ulcer may be definitely established or ruled out by an adequate history and careful radiographic studies. There is, however, a sizable group of patients in whom some or all of the findings are equivocal, and in whom additional diagnostic measures may be useful. Study of the basal, or caffeine-induced gastric, secretion may offer considerable aid, but these tests have not been widely used. The authors have attempted to simplify the caffeine test for possible use as a routine procedure.

The test, which is most likely to aid in the diagnosis of individual cases, appeared to be the caffeine test devised by Roth, Atkinson, and Ivy, the value of which has been confirmed by Roth in further studies and by others. Although earlier investigators had studied the effect of caffeine

on gastric secretion in man, Roth and coworkers pointed out that the peak of the stimulating effect had not been observed because of the long latent period before response begins.

The test was performed on 130 subjects, all of whom were private patients under the authors' investigation for gastrointestinal complaints. There were 48 patients with duodenal ulcer and 82 control patients. The age and sex distributions are given.

Great care was taken in each case to establish the presence or absence of duodenal ulcer, and all cases in which significant doubt remained were rejected from this study. Each case was reviewed in detail to ascertain the presence or absence of typical ulcer symptoms and to evaluate the response to treatment. The x-ray films were evaluated as to the presence or absence of a crater and deformity of the duodenal bulb. A minimum of seven views of the duodenal bulb were available in each case.

The decisions on the clinical and radiographic evidence were made without knowledge of the results of the test in order to avoid prejudice and, in all of the cases presented, were unanimous.

The results by single aspiration technique confirm clearly the finding of previous investigators that caffeine causes a more sustained and higher output of gastric acid in duodenal ulcer patients than in patients without ulcer. Data from this study indicate that the group difference may be great enough to merit consideration of this test as an aid in the diagnosis of duodenal ulcer. Any possible diagnostic use would require careful consideration of false positive and false negative responses.

A simple caffeine gastric analysis is described, using a test meal consisting of 0.5 gm. of caffeine with sodium benzoate in 200 cc. of water. The gastric contents are evacuated with an Ewald tube 90 minutes later and a sample titrated in the conventional way. (Littman, A., et al., A Single Aspiration Caffeine Gastric Analysis in Duodenal Ulcer and Control Patients; *Gastroenterology*: 28: 953-963, June 1955)

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### Capillary Hemangiomas of the Skin

This article is concerned with follow-up observations of a group of untreated capillary hemangiomas, an anomaly which is encountered often enough in pediatric practice to be of some importance. It is emphasized that the hemangiomas studied in this report include only the capillary type. Other terms include "arterial hemangioma" and "strawberry nevus." The "port-wine" stain, sclerosing hemangioma, spider angioma, lymphangioma, hygroma, cirroid aneurysm, and diffuse visceral hemangiomas are not included.



In the present series of 52 consecutive cases, no lesions, which were predominantly cavernous in type, were encountered; however, four capillary hemangiomas with a partial cavernous component are included.

Despite such strong agreement concerning the management of infantile hemangiomas, there have been a few reports to the effect that these lesions are not as dangerous as many authors have indicated. Lister, in 1938, reported a series of 77 patients with 92 capillary hemangiomas (which he identified as "strawberry nevi") that were followed without treatment for various periods up to 7 years. Of these, 49 entirely disappeared, 38 were definitely showing regression and were still under observation at the time of this report, and 5 showed beginning retrogression when they were lost to follow-up. Lister emphasized that the natural history of the hemangioma is one of rapid growth for 6 months to one year, with subsequent spontaneous retrogression. He considered it remarkable that "strawberry nevi," which are common in infants, are seldom seen in school children or adults. He made the cogent observation that the spontaneous regression of these lesions may well explain the uniformly good results recorded following treatment, whatever may be the method advocated.

Since 1947, a total of 42 consecutive patients with 52 capillary hemangiomas have been examined at regular intervals. The follow-up results in this series have so fully corroborated the observations of Lister and are so markedly at variance with the observations of those who advocate vigorous treatment of all hemangiomas of this type, that a report of these patients seems indicated.

The results in this group of 52 capillary hemangiomas would seem to indicate that vigorous treatment is not necessary in every case. When an infant is seen at birth with a small capillary hemangioma which can be easily destroyed or excised without deformity, it follows that this should be done rather than to allow the lesion to increase in size. Eleven were excised when first seen. All but one of these were seen at an early stage of their disease, and with lesions which were either small enough to permit treatment without deformity or were located in areas where treatment could be administered without resultant serious deformity. At the Ellis Fischel Cancer Hospital (Columbia, Mo.) these children were often seen, however, at a time when their hemangiomas had reached a late stage of development. Thus, 41 hemangiomas were first seen at a time when the lesion was adjudged to be too large for treatment without deformity, or was situated in an area where it was believed that treatment would produce undue deformity. The fact that 24 of these completely regressed without treatment and that an additional 14 are at present undergoing definite and continuing regression is strong evidence that not all hemangiomas need to be treated.

A surprising lack exists of well-documented and well-followed series of capillary hemangiomas in the literature, both with and without treatment. Many authors have emphasized that rapid growth is a common characteristic of the capillary hemangioma. However, lack of follow-up of an appreciable number of patients without treatment seems to have prevented the equally important observation that the growth of most of these lesions is limited to a period of not over one year, with subsequent regression thereafter. From the data in this series, it appears that regression can be depended upon in the majority of cases. Not a single patient was endangered by adoption of a conservative observation-only policy, a fact that should be emphasized in order to prevent overtreatment in some of these cases.

The fact that none of the 52 hemangiomas occurred in children over 7 years of age and that none was observed in adults is further evidence that spontaneous regression must be the rule.

It is emphasized that ideal treatment of infantile capillary hemangiomas consists of destruction or surgical excision early in life before the characteristic rapid growth occurs. The fact remains, however, that many lesions will be seen after enlargement has occurred, and it appears that these may be followed closely without treatment. It is probable that judicious restraint may produce a much better end result than that following well-meant but vigorously applied destructive methods of treatment. There is need for additional reports of conservatively managed cases in order to determine the true natural history of these lesions. (Modlin, J. J., Capillary Hemangiomas of the Skin: Surgery, 38: 169-179, July 1955)

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#### Diagnosis, Treatment, and Prognosis of Roentgen Ray Injuries to Dentists

The problem of roentgen ray injury to the dentist is similar to that of such injury to the physician. Too often the only qualification deemed necessary to practice roentgenology is the possession of roentgenologic apparatus. Even if the average physician or dentist takes the time and trouble to acquaint himself with the hazards of roentgen ray exposure and the means of prevention, he only too frequently forgets what he has learned, or develops a daredevil disregard for the danger. The onset of changes in the skin is frequently so insidious that irreparable damage is often done before the condition is recognized.

At the Mayo Clinic, 140 physicians, 52 dentists, one osteopath, and one physician's wife, in whom roentgen ray dermatitis of the hands developed as a result of their occupational exposure to roentgen rays,



have been seen. The youngest physician so injured was 29 years of age, and the oldest was 75 at the time they were first examined at the Mayo Clinic. The average age of the physicians was 55 years. The youngest dentist with roentgen ray dermatitis was 34 years of age and the oldest was 66 years. The average age of this group was 52 years.

Whereas most physicians received roentgen ray injuries through making prolonged fluoroscopic examinations without proper precautions being taken against overexposure, the dental group received their injuries by holding the films in the mouths of patients while getting roentgenograms of the teeth. In the latter group, it was the index finger and thumb of one or both hands that were most frequently involved.

Of the group of 194 patients with chronic roentgen ray dermatitis of the hands, 61, or 31%, experienced malignant degeneration of the lesion. Although only one physician and one dentist are known to have died as a result of the disease, others must have succumbed because metastases were present in two physicians and three dentists at the time of their examination.

An overdose of radiation of the skin results in either acute or chronic roentgen ray dermatitis. Whether the condition is acute or chronic depends on the manner in which the overdose is received. The acute reaction may be due to a single massive dose, intentional or otherwise, or to several exposures at short intervals. It may be an expected reaction which accompanies massive irradiation used in an attempt to eradicate an underlying malignant growth, and, in such a situation, it is a justifiable occurrence. Too often, however, an acute radiation burn follows a prolonged fluoroscopic examination or an accidentally delivered overdose; it is these instances that should be avoided.

Whereas acute roentgen ray dermatitis is the result of a single massive dose or frequent doses at short intervals, chronic roentgen ray dermatitis is the result of many exposures over a long time. This chronic form may be observed after the treatment of such conditions as acne, psoriasis, and warts, but is most frequently observed on the hands of physicians and dentists who are doing roentgenographic examinations without taking proper precautions. The onset of the dermatitis is insidious, without pain or erythema to call attention to the recipient that certain skin changes are occurring which may ultimately affect his limb or even his life.

The best treatment for chronic roentgen ray dermatitis is preventive in character. No matter what the calibration of his machine may be, a physician or dentist is wise who never exposes himself or his hands to roentgen rays.

A technic for taking dental roentgenograms wherein the technician is almost completely eliminated from the hazard of any exposure has been developed at the Mayo Clinic. The patient holds the film in his own mouth while the operator steps behind a leaded partition to make the exposure.

The patient cannot possibly suffer from the minimal dose received, but the operator could suffer from accumulated doses if he exposed himself to them. A further precaution taken at the clinic is the compulsory annual examination of the hands of all personnel whose daily work entails any possible exposure to radiation damage.

Once chronic roentgen ray dermatitis has become established, it is imperative that further exposure to roentgen rays be avoided. The hands should be examined every 6 months by a competent dermatologist. Complete removal of keratotic areas by fulguration usually will prevent carcinomatous degeneration. Trauma or infection may produce ulceration in a hyperkeratotic area, and when this occurs, wide excision to healthy skin and the placing of a skin graft may easily effect a cure. When there is even the slightest suspicion that malignant degeneration may be present, a biopsy should be performed. The degree of malignancy and the location of the lesion will determine whether excision and a skin graft or amputation is the treatment of choice. To temporize and try to save a digit when amputation could be performed might result in metastasis and death.

It seems reasonable to expect that a third of all patients with chronic roentgen ray dermatitis will develop malignant degeneration. When metastasis to regional lymph nodes occurs, the prognosis is grave. (Young, H. H., Kunkel, M. G., Diagnosis, Treatment and Prognosis of Roentgen Ray Injuries to Dentists: J. Am. Dent. A., 51: 1-7, July 1955)

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### Sedation for Ophthalmic Surgery

Despite regional blocks, retro-bulbar injections, and preoperative barbiturate sedation, intra-ocular surgery can still be a hazardous procedure. Apprehension and the accompanying general increase in muscle tone, which enhance the risks of such operations as intra-capsular cataract extraction, are only partially overcome by these methods. General anesthesia, with its tendency to venous congestion in the head and vomiting on recovery, offers no solution. Any method of sedation which will induce mental and physical relaxation in a tense and apprehensive patient, without the disadvantages of general anesthesia, would be of great value.

Experience with chlorpromazine, promezathine, and pethidine in premedication for general anesthesia suggested that a combination of these drugs might fulfil the requirements of ocular surgery. Patients who were given the mixture showed, at the time of induction, an absence of apprehension and a degree of mental and physical relaxation not found with barbiturate sedation, and their postoperative recovery was remarkably free from restlessness and untroubled by the nausea, vomiting, and respiratory depression which tends to accompany sedation with opiates.



Operations under local anesthesia, using this method of sedation, were performed on 89 patients. The majority of cases were given chlorpromazine (50 mg.), promezathine (50 mg.), and pethidine (100 mg.) by the intravenous route. In a few cases, a smaller dose in the same proportions was given and in 16 cases the intramuscular route was used. This dosage had already been used satisfactorily as premedication for general anesthesia in a large number of cases. No other form of sedation was used. When using the intravenous technique, the drugs were given 20-30 minutes before the operation. The dose of all three substances was diluted in 20 ml. saline and injected very slowly. As the importance of slow administration became evident, a minimum period of 10 minutes was adopted for the injection. In this way, the progress of pulse and blood pressure could be watched and administration stopped if the full dose seemed likely to have too great an effect. When using the intramuscular route, the full dose was given 1-2 hours before the operation.

In all cases, local anesthesia was used exactly as with luminal sedation. For intra-ocular operations, surface anesthesia with 4% cocaine drops was combined with a facial nerve block, lid stitch injections, and a retrobulbar injection of 1.5 ml., using 5% procaine or 2% xylocaine with adrenaline 1:40,000. For other operations, local infiltrations according to standard procedures were used. Two operations for squint in adults were done under surface cocaine only.

The appearance of patients under the influence of these drugs is characteristic. They lie quietly and appear to be asleep. According to the depth of sedation, they may answer questions and obey orders easily, or they may snore and be apparently unrousable, though they always show some response to painful stimuli. There is a marked pallor of the face and bloodlessness of the lips which may be alarming unless it is expected, and the skin is noticeably cold to the touch.

When the intravenous route is used, there is a tendency to severe temporary tachycardia unless the injection is given very slowly. It lasts no longer than 10 to 15 minutes as a rule and no case of collapse has occurred, but it may be alarming to both the patient and the anesthetist. In order to reduce both the tachycardia and the fall in blood pressure, the injection should be given evenly and slowly over a period of 10 to 15 minutes. With this technique, no difficulties have been encountered. When the intramuscular route is used, both tachycardia and hypotension are minimal. The fall in blood pressure has been well tolerated but it was thought best to keep the patients lying flat until it began to rise again.

The method is entirely safe in the hands of an anesthetist with experience of these drugs. None of the present series of cases gave cause for anxiety, and the method has been used by one of the authors with no unfavorable reactions in over 500 cases as premedication for general anesthesia.



The toxic effects of chlorpromazine have been reported mainly in cases undergoing prolonged courses of the drug for psychiatric purposes, and no case of a dangerous reaction to a single dose, given for anesthetic purposes, is known to the authors. Nevertheless, known liver disease and severe diabetes have been considered to be a contraindication to its use so far. (Burn, R. A., Hopkin, D. A. B., Edwards, G., Jones, C. M., Sedation for Ophthalmic Surgery: Brit. J. Ophth., XXXIX: 333-336, June 1955)

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### Public Relations in Naval Hospitals

Public relations may be simply defined as the art of helping people or institutions who deserve good public opinion to achieve the reputation they deserve. This is definitely applicable to Naval Hospitals.

Throughout the history of the medical department of the Navy, excellent medical care has been rendered to patients in Naval Hospitals. However, the best public opinion, as the result of effective treatment of the patients, has not always been obtained.

Why?

Primarily, the cause is lack of mutual understanding between the staffs and their public, the patient.

The satisfaction of the patient cannot be overstressed. It is an "all hands" responsibility which requires effort by all military and civilian personnel of each command.

The impression the patient gains as he enters the hospital gate, as he is received in the outpatient department or at the information or admission desk is lasting. First impressions or opinions are strong and hard to change.

Lack of information results in the lack of understanding. Accordingly, the informed patient becomes satisfied because of his knowledge or understanding of details pertinent to him and his case. For example, a patient to be surveyed, when informed of the simple facets of the procedure, will understand his case and appreciate the interest shown him.

Each patient, during his hospital stay, should have a "sense of belonging," just as he had at his duty station before admission. This sense or feeling will be transferred to each person who visits the patient, for the patient then becomes, in effect, a member of the hospital's public relations department.

The use of effective public relations in a naval hospital is the means, and the good relationships achieved are the ends in obtaining a good and deserved reputation. (BuMed Information Memo, Vol. 6, No. 7)



Oxygen Administration in Retrolental Fibroplasia

The Advisory Committee on Retrolental Fibroplasia to the California State Department of Public Health strongly urges that the following policies with respect to oxygen administration be adopted at once by all hospitals caring for the newborn:

- 1 Oxygen should be administered to premature infants only on the specific order of a physician.
- 2 Oxygen should not be administered in concentrations exceeding 40%, and should be discontinued as soon as the infant's condition permits. Cyanosis and respiratory distress may occasionally require oxygen concentrations exceeding 40% for short periods of time.
- 3 The prescription for continued oxygen therapy should be renewed daily by the physician.
- 4 The actual concentration of oxygen during administration should be checked with an oxygen analyzer at least every eight hours.
- 5 When oxygen is administered for periods longer than three days, the oxygen concentration should be measured more frequently to be sure that it never exceeds 40%.
- 6 The continuous administration of oxygen for periods in excess of three days should be prescribed only in exceptional circumstances.

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Training Duty Courses for U. S. Naval  
Reserve Dental Officers

Dental Reserve Officers who desire training duty in fiscal year 1956 may avail themselves of the several courses listed below. Quotas provided for each District have been increased over last year in most instances, with pay and allowances for eligible Reservists. Training duty may also be performed without pay and allowances, but for the earning of promotion and retirement points. Any desired information may be obtained from the District Commandants.

Dental Military Training - 12 days. To be conducted in the Naval Dental School, National Naval Medical Center, Bethesda, Md., October 3-15, 1955 and March 4-17, 1956. The first week is devoted to professional subjects concerning the Reserve Program. The second week will be devoted to the Medical Aspects of Special Weapons and Radioactive Isotopes, with emphasis on basic concepts of atomic medicine.

Dental Military Seminar - 3 days. Convened concurrently with the American Dental Association meeting, San Francisco, Calif., a dental-military seminar to acquaint Reserve Dental Officers with the latest information on subjects of a dental military nature.

Seminar, Commanding Officers of Naval Reserve Dental Companies - 6 days. Convenes in the Bureau of Medicine and Surgery, Washington, D. C. This seminar provides indoctrination and orientation in the organization, administration, and operation of the Navy Dental Department from the Bureau level, and to acquaint the trainee with current concepts and trends affecting the Naval Reserve Program, with emphasis on the Reserve Dental Program.

Special Weapons, Isotopes and Professional Subjects - 5 days. To be conducted at the U.S. Naval Station, Treasure Island, San Francisco, Calif., February 27, 1956, for the 11th, 12th, and 13th Naval Districts. An up-to-date review of problems and information relating to the various medical aspects of special weapons and radioactive isotopes, with primary emphasis on their application to military and naval dentistry and civil defense will be presented.

Ensign 1995 (Dental) Training. To be conducted at U.S. Naval Dental Clinics and Facilities during the first quarter fiscal year 1956. This will present training in the professional services at naval dental clinics and facilities, including indoctrination in Navy Medical Department operations and administration pertaining to military dentistry.

Dental Ensign Orientation Program - up to 60 days. Convened at Naval facilities authorized by BuMed, to provide training and orientation for Ensigns 1995 (Dental) in Naval dental clinics, training centers and other Naval dental facilities. This training will enable the Bureau to order the Ensign 1995 to immediate active duty upon graduation. (DentDiv, BuMed)

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### "Commendation"

The Commander Fleet Air Quonset has commended Captain J. L. Enyart, MC USN, Commanding Officer of the U.S. Naval Hospital, Newport, R.I. The commendation reads:

"Frequently during the past 15 months, the efficiency of performance of the U.S. Naval Hospital, Newport, under the command of Captain John L. Enyart, MC U.S. Navy, has been brought to the attention of this command. Particularly, during the period of the BENNINGTON disaster in May 1954, when helicopters transported hundreds of seriously and critically injured naval personnel to the hospital, the patients were treated with great despatch and skill resulting in many lives being saved. From personal observation and many commendatory comments and letters, the performance of all of the personnel during this tragedy reflected outstanding training and ability to cope with any emergency.

This remarkable record of achievement is due, in great part, to the outstanding and efficient leadership of Captain John L. Enyart, MC, U.S. Navy.

Commander Fleet Air Quonset (SOPA Narragansett Bay) commends Captain Enyart for his able leadership and exceptional professional skill and requests that this letter be made a permanent part of his official record. "

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### Retirements

RADM C. A. Swanson MC USN  
CAPT L. T. Dorgan MC USN  
CAPT T. Q. Harbour MC USN  
CAPT E. R. Hering Jr. MC USN  
CAPT M. M. Maxwell DC USN  
CAPT F. A. Richison DC USN  
CAPT C. W. Shilling MC USN

CAPT H. O. G. Wagner MC USN  
CDR B. R. Evans NC USN  
CDR J. D. Hodge NC USN  
LT M. J. Grande NC USN  
LT R. Mallen NC USN  
LT G. F. Pierce MSC USN  
LT R. L. Smith MSC USN

LTJG T. A. Michael NC USN

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## MEDICAL RESERVE SECTION

### Medical Department Correspondence Course Program

The Correspondence Course Training Program of the Medical Department was originally established as an organic division of the Bureau of Medicine and Surgery in 1948. It was created, primarily, to maintain the Reserve forces in a more efficient state of readiness for recall to active duty with the regular Navy and, in addition, to provide the inactive Reservist with the necessary means to earn point credits for promotion and retirement under Public Law 810 of the 80th Congress.

While Correspondence Course Training was originally conceived for the exclusive training of the Reserve components, it has been subsequently enlarged to include regular Navy personnel and also members of other services of the Armed Forces. A further increase in the number of enrollees is anticipated when promotion of officers of the regular Navy will be based upon Correspondence Courses submitted in lieu of the usual written examinations presently required.

Correspondence Course study within the Naval Establishment is no mere accident as the value of this type of self-instruction has been long and well established. Over 5000 leading industrial corporations, railways, banks, manufacturing concerns, department and chain stores think so highly of correspondence study that each has a contractual relationship with various home study schools for the purpose of training their employees for advancement and promotion. Most leading colleges and universities offer correspondence course study as a means of obtaining credit toward academic degrees. The list of Correspondence Courses available is endless. Aside from being an effective method of instruction, correspondence course study offers certain distinct advantages: (a) The student is encouraged to form his own judgment. (b) He can do all the work himself. (c) He can work alone and independently. (d) He can concentrate uninterruptedly. (e) He can control his own time and speed of work. (f) He can secure courses in which he is interested but which are otherwise unavailable. (g) He assumes considerable responsibility for his own progress.

Correspondence Courses available to Medical Department personnel are of two categories: (1) the basic or general courses administered by the Bureau of Naval Personnel, of which there are fifteen, such as,

Navy Regulations  
Naval Orientation  
Leadership

Personnel Administration  
Security of Classified Matter  
Uniform Code of Military Justice



These courses are available to all Medical Department officers, Chief Petty officers, and those enlisted personnel so recommended by their commanding officers. Requests for enrollment in these courses are made to the U. S. Naval Correspondence Course Center, Building R. F., U. S. Naval Base, Brooklyn 1, N. Y.; and (2) the professional courses administered by the Bureau of Medicine and Surgery, of which there are fourteen:

Medical Department Orientation	Combat and Field Medicine Practice
Insect, Pest, and Rodent Control	Tropical Medicine in the Field
Clinical Laboratory Procedures	Radiological Defense and Atomic Medicine
Special Clinical Services	Submarine Medicine Practice
Pharmacy and Materia Medica	Frigid Zone, Medical and Dental
Functions of Officers of the Medical Department	Practice
Naval Preventive Medicine	Aviation Medicine Practice
	Special Clinical Service

The first five professional courses are available to Medical Department officer and enlisted personnel; the remaining nine courses are available to officer personnel only. Requests for enrollment in these courses are made to the Commanding Officer, U. S. Naval Medical School, National Naval Medical Center, Bethesda 14, Md.

Retirement point credits are given to eligible members of the Naval Reserve not on active duty for the satisfactory completion of appropriate correspondence courses not to exceed 60 points per year. It is recommended that officers divide their promotion points equally, insofar as practicable, between basic and professional courses.

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#### From the Note Book

1 Rear Admiral B. W. Hogan, Medical Corps, USN, the Surgeon General of the Navy, attended a three-day meeting of about 170 top-level civilian and military leaders of the Department of Defense, July 14-17, at the Marine Corps School, Quantico, Va.

Similar to conferences held at Quantico in July 1953 and June 1954, the "Secretaries' Conference" is conducted to afford an informal meeting place for discussions of matters of common interest and a general exchange of ideas among Defense leaders. (TIO, BuMed)

2 Captain B. F. Avery, MC USN, was designated Director of the Armed Forces Medical Publication Agency on July 1, 1955. He is also Director of the Publications Division, Bureau of Medicine and Surgery. Captain Avery, as Director of the Agency, is the Editor of its publications, the

United States Armed Forces Medical Journal and the Medical Technicians Bulletin. (TIO, BuMed)

3 The Research Advisor to the Surgeon General of the Navy, Doctor Howard T. Karsner, has been appointed as the General Consultant of the Medical Advisory Board of the Leonard Wood Memorial (American Leprosy Foundation). (TIO, BuMed)

4 Captain T. J. Canty, MC USN, Chief of the Amputee Service, Naval Hospital, Oakland, Calif., was recently lauded for his participation in the field of rehabilitation by the Mexican and Colombian governments. Captain Canty attended a rehabilitation symposium at Bogota, Columbia, and provided rehabilitation consultation to the Mexican government at Mexico City. The President of Columbia presented the Colombian Jose Fernandez Madrid Medical Award (subject to the approval of the U. S. Congress) to Captain Canty for his excellent and meritorious service to that country in the field of rehabilitation. (TIO, BuMed)

5 The Naval Hospital, Guam, M. I., successfully completed the first military-medico symposium conducted by the Navy medical department outside the continental limits of the United States. The symposium was held June 21-23, and marked the first such conference ever held there.

6 The weekly CBS TV series entitled, "Navy Log," is now being produced for nationwide showing commencing September 20, 1955. The series will tell a story of teamwork and tradition of the Navy by dramatizing true episodes. (TIO, BuMed)

7 Cardiovascular Disease--Data on Mortality, Prevalence and Control Activities is a new publication of the Public Health Service. Designed particularly for use by people working in the heart disease field, the booklet provides information on cardiovascular-renal disease mortality and prevalence, and on heart disease control activities. (P. H. S., D. H. E. W.)

8 Nine laboratory refresher courses covering the serology of syphilis, management and control of syphilis serology by the regional laboratory, and tests for syphilis, using the *Treponema pallidum*, will be offered at the Venereal Disease Research Laboratory in Chamblee, Ga., from September 1955 through May 1956. (P. H. S., D. H. E. W.)

9 Approximately 720,000 cc's of poliomyelitis vaccine, produced by Eli Lilly Company, have been released by the Public Health Service. As a result of this action, a total of approximately 2,558,000 cc's of poliomyelitis vaccine has been released since adoption of the revised testing requirements on May 26. (P. H. S., D. H. E. W.)



10 A discussion of salvage methods based on established principles of reconstruction in secondary reconstruction of the hip joint appears in Surg. Gynec. & Obst., July 1955; C.F. Ferciot, M.D.

11 Roentgenographic and gastroscopic examinations, when applicable, remain the most important and reliable methods available in diagnosis of gastric lesions; the brush technic may assist in establishing a diagnosis of malignant disease, particularly when the mucosal surface is involved and the lesion is within the field of the brush. (Gastroenterology, June 1955; D.C. Brown, M.D. et al.)

12 A method is described, which appears to be highly effective, in isolating in a relatively simple manner large numbers of "L. E." cells from a single drop of finger blood of a lupus patient. (Blood, July 1955; I. Snapper, M.D., D.J. Nathan, M.D.)

13 Four cases of right-sided total hemispherectomy in adults are described. The entire hemisphere was removed with the exception of the thalamus and hypothalamus. (Surgery, July 1955; G.M. Austin, M.D., F.C. Grant, M.D.)

14 The problem of reducing the number of victims from automobile accidents depends on the over-all education of the public, improved law enforcement, first aid instruction, and improved safety engineering of the modern automobile. (Indust. Med., July 1955; R.W. Zollinger, M.D.)

15 Fifty consecutive male Air Force Recruits with pulmonary calcification, the majority of which were multiple miliary lesions, were subjected to clinical study and scalene node biopsy. The place of residence and skin tests results indicated that the majority of these calcifications were probably of histoplasmic origin. (Am. Rev. Tuberc., July 1955; J.E. Johnson, Jr., M.D.)

16 Peru Farver, a Choctaw Indian and veteran of 45 years of service with the Department of Interior's Bureau of Indian Affairs, has been appointed to the staff of the newly organized Division of Indian Health. In his new position, Mr. Farver will serve as advisor to the Public Health Service on relations with the Indian and Alaska native populations and their tribal councils. (P. H. S., D. H. E. W.)

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The printing of this publication has been approved by the Director of the Bureau of the Budget, 16 May 1955.

BUMED NOTICE 6780

11 July 1955

From: Chief, Bureau of Medicine and Surgery  
To: Holders of BW Field Sampling Kit, E25R1

Subj: BW Field Sampling Kit, E25R1; potential operational defect in

This Notice informs holders of the BW Field Sampling Kit of a potential operational defect in subject item and recommends a method to help prevent improper operation of the kit.

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BUMED NOTICE 7303

11 July 1955

From: Chief, Bureau of Medicine and Surgery  
To: All Activities Under Management Control of the Bureau of  
Medicine and Surgery

Subj: Recording and Reporting of allotment obligations pursuant to  
Section 1311 of Public Law 663

Ref: (a) NavComptInst 7303.5 dated 26 May 1955

This Notice invites attention to reference (a) and provides advance information concerning reporting and certification of obligations as of 30 June 1955.

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BUMED INSTRUCTION 6710.16

21 July 1955

From: Chief, Bureau of Medicine and Surgery  
To: All Ships and Stations

Subj: Defective medical and dental material; authority for disposition of

Ref: (a) Medical and Dental Material Bulletin, Edition No. 56  
dtd 1 July 1955  
(b) Art. 25-21, ManMed Dept

This Instruction provides authority for the disposal of defective material listed in paragraph IV of reference (a).

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## PREVENTIVE MEDICINE SECTION

### Insect-Borne Virus Diseases of Military Importance

There are more than 15 insect-borne virus diseases which require consideration in different parts of the world, but only 3 of them, yellow fever, dengue and sandfly fever, have thus far affected sufficiently large numbers of troops to be regarded as important from the numerical point of view. Others like Japanese B or Russian Spring-Summer encephalitis, which produce clinically manifest disease in only small numbers, may become significant either because of the high case fatality rate or as problems in diagnosis and management. Thus, since 1951, there have been 17 deaths from Japanese B encephalitis among American military personnel and their dependents in Okinawa, Japan, and Korea. In recent years, there have been outbreaks of a disease, called Central European encephalitis, from which viruses have been recovered that are either closely related or identical with the tick-borne virus responsible for the Russian Spring-Summer encephalitis of the Siberian forests. The great influx of immigrants to Israel has brought to light the fact that epidemics of dengue-like fever in the Middle East can be caused by the mosquito-borne West Nile fever virus, and experimental tests of this virus as a possible therapeutic agent in cancer patients revealed that it can also cause encephalitis.

Yellow fever is no longer a threat to military operations in endemic areas because a successful vaccine provides a means of adequate control, but constant vigilance and appropriate mosquito control measures are required to keep it confined to its jungle reservoirs. Dengue fever remains an important potential problem, particularly in the Western Pacific Islands, Formosa, South China, Indochina, India, Malaya, Indonesia, and northern Australia, but the recent development of experimental vaccines capable of immunizing human beings against both known immunologic types of the virus offers new possibilities of control where mosquito abatement may be difficult or impractical. New serologic tests, based on the demonstration of antibodies for the hemagglutinins associated with the dengue viruses, provide a means for both rapid diagnosis and epidemiologic survey. Sandfly

fever, which presents a problem in those areas of Europe, Africa, and Asia lying between 20 and 45 degrees north latitude where Phlebotomus papatasi is prevalent, has become much more manageable in recent years, not only because of the remarkable effect of DDT on the vector, but also because the successful adaptation of the two known immunologically distinct viruses to newborn mice is providing new tools for diagnosis, epidemiologic survey, and human vaccination.

The purpose of this communication is (1) to call attention to the insect-borne virus diseases in different parts of the world, and (2) to discuss some of the new developments in the diagnosis, the epidemiology, and the prevention of some of these diseases. While there are more than 15 insect-borne viruses that are pathogenic for man, different ones need to be considered in different parts of the world (Table I). Thus, in the United States and Canada we are concerned with four such virus diseases. Three of them, i. e., St. Louis, western equine, and eastern equine encephalitis, are mosquito-borne; and the fourth, Colorado tick fever, is, as the name implies, a tick-borne infection which thus far has been limited to the Rocky Mountain region of the United States. In the western hemisphere, south of the United States, one needs to consider yellow fever, dengue, and the, as yet, little known Ilheus virus which has been discovered in the Bahia area of Brazil. The Venezuelan, eastern and western equine encephalitis viruses are also known to be present in certain parts of South America. Until recently, it was generally believed that there were no insect-borne virus diseases of man in the central and eastern regions of Europe. In recent years, however, an entity which has come to be called Central European encephalitis, has been recognized in Czechoslovakia and Austria and probably occurs also in other contiguous areas. Clinically, the disease is similar to the Far Eastern Russian tick-borne encephalitis, and the viruses which have been recovered from patients by several investigators appear to be closely related to, if not identical with, the Russian Spring-Summer Encephalitis-Louping-Il family of viruses. In the Mediterranean and Adriatic areas of Europe, sandfly (pappataci or phlebotomus) fever has long been known to be endemic, and at various times has been a threat to military operations in these regions. In the Middle East and the Near East, sandfly fever has long been recognized as a problem in military medicine, and recent observations on the West Nile fever virus indicate that it will also have to receive special consideration. Further south in Africa three well-known viruses require consideration in their own particular endemic regions. These are yellow fever, West Nile fever and Rift Valley fever, although there is some question as to whether the last named is ordinarily transmitted to human beings by insects. In addition to these better known viruses, there is another group of 7 viruses, all of which have been recovered in the Uganda area of Africa. These are Ntaya, Zika, Uganda S, Bwamba, Bunyamwera, Mengo, and Semliki forest. It is known that these viruses infect human beings,



Insect-Borne Virus Diseases in Different  
Parts of the World  
Table I

Region	Viruses
U. S. A. and Canada	St. Louis, Western equine and Eastern equine encephalitis; Colorado tick fever (limited area). (Encephalomyocarditis--Mengo)?
Western Hemisphere--south of U. S. A.	Yellow fever, Dengue, Ilheus (Brazil) Venezuelan, Eastern and Western equine encephalitis
Europe--central and eastern	Central European encephalitis (Russian encephalitis--"Louping-III" tick-borne family of viruses)
Mediterranean, Adriatic, Near East, Middle East	Sandfly fever, West Nile fever
Africa--south of 20°N. Lat.	Yellow fever, West Nile fever, Rift Valley fever (Ntaya, Zika, Uganda S, Bwamba, Bunyamwera, Semliki forest, Encephalomyocarditis--Mengo)
Far East and southwest Pacific	Dengue, Japanese B encephalitis (Murray Valley encephalitis)
Russian Far Eastern Provinces--Siberia, Vladivostok and area bordering Sea of Japan	Russian spring-summer, tick-borne encephalitis Japanese B encephalitis

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but the extent to which these infections are inapparent is not known, nor is the type of disease, if any, which they might produce under natural conditions, known.

In the Far East and Southwest Pacific, there are only two viruses which need to be considered, although recent serologic surveys in India have raised the question of the possible occurrence of some of the African viruses in Asia. The two viruses which have been proved to cause disease in this part of the world are Japanese B encephalitis and dengue. The recent recovery of the so-called Murray Valley encephalitis virus in Australia brings to light an agent that may only represent a slightly different antigenic type of the Japanese B encephalitis virus. In the far-eastern provinces of the U. S. S. R., the Russian Spring-Summer tick-borne encephalitis is the only insect-borne virus currently known to affect human beings, except in Vladivostok and the adjacent areas bordering on the Sea of Japan, where Japanese B encephalitis is prevalent.

Although this list appears to be large, past experience has shown that only a few of these insect-borne virus diseases may be important from a military point of view. There are, perhaps, two main categories of diseases which may be regarded as being of military importance. In the first and more significant category, one must consider the diseases which affect sufficiently large numbers of people to become a threat to military operations in endemic regions. In the second and less significant category, belong those infections which produce clinically manifest disease in only small numbers of individuals but become important because they are associated with a high case fatality rate or because they may present special problems in diagnosis or management. On the basis of past experience, only three insect-borne virus diseases, yellow fever, dengue, and sandfly fever, can be regarded as belonging to the first category. In more recent years, yellow fever has been removed from this category by the development of an effective vaccine, and during World War II, only dengue and sandfly fever affected sufficiently large numbers of troops to be important from a numerical point of view. One of the main reasons that these three insect-borne virus diseases belong to this particular category is that almost all infections with these viruses are clinically apparent in those human beings who move into the endemic regions from parts of the world where these viruses do not occur. The other insect-borne virus infections belong to the second category. Except for Rift Valley fever, the vast majority of human infections with the viruses in this category are clinically inapparent. It is possible, however, that under certain conditions some of the recently discovered viruses about which relatively little is known, might achieve special importance for foreign troops operating in endemic areas.

The present status of the three viruses which belong to the first category of military importance are considered first. While yellow fever is no longer a threat to military operations in endemic areas because the



availability of a good vaccine provides a means of adequate control, constant vigilance and appropriate mosquito control measures are required to keep this disease confined to its jungle reservoirs in Africa and the Western Hemisphere. The recent appearance of yellow fever in the Caribbean area serves to emphasize the need for continued control of Aedes aegypti in all cities which serve as ports of call for airplanes and ships from endemic regions.

Dengue fever remains an important potential problem, particularly in the southwestern Pacific islands, Formosa, South China, Indochina, India, Malaya, Indonesia, and northern Australia. These are known endemic regions of this infection by virtue of past experience, actual recovery of dengue viruses, or demonstration of a high incidence of antibody among the natives. The potential spread of dengue from these endemic foci to non-endemic areas was demonstrated in a most remarkable way in Japan during World War II, when it is estimated that as many as two million cases of the disease occurred in the port cities of Nagasaki, Kure, Sasebo, Kobe, and Osaka. According to estimates furnished the author by the Japanese public health officers of Osaka, that city with a population of two million had 400,000 to 600,000 cases of dengue during the summer of 1944. In addition to the endemic areas just listed, there are undoubtedly others about which information is currently unavailable. Simple, new serologic methods have recently been developed for the detection of antibodies against the dengue viruses. By means of these tests it is relatively easy quickly to determine whether or not the known dengue viruses are endemic in a given area. Among the ten strains of dengue virus which were recovered during World War II from New Guinea and India, representing endemic areas, and from Hawaii and Japan, representing areas with imported epidemics, only two distinct immunologic types were found to be present. It has now been shown that each of these viruses is associated with a specific hemagglutinin for chick erythrocytes and that, during the course of the infection, human beings develop antibodies which inhibit the activity of this hemagglutinin. These hemagglutination-inhibition antibodies provide a very rapid and simple tool, not only for the specific diagnosis of infection but also for epidemiologic survey. Thus, tests on 20 adult human sera from Malaya and 10 such sera from Borneo quickly established that dengue had occurred in these areas. Only 0.1 cc. of serum is required for such a test and the answer can be obtained in a few hours. By means of the hemagglutination-inhibition test, it is now possible to confirm the diagnosis of dengue within 24 hours after the temperature has returned to normal. Only by further work on febrile dengue-like illnesses in suspected endemic areas, will it be possible to establish whether or not additional immunologic types of dengue virus are in existence.

During World War II, one immunologic type of dengue virus, which was adapted to mice, yielded a mutant which lost its capacity to produce

the febrile systemic illness in human beings but retained its capacity to immunize against the unmodified virus. In recent years, the second immunologic type of dengue virus was shown to yield a similar mutant capable of producing immunity in human beings. A vaccine utilizing these two mutant viruses offers new possibilities of control where mosquito abatement may be difficult or impractical. Experiments which are now in progress would indicate whether it will be possible to immunize against body immunologic types of the virus by injection of a mixture of the two or whether it will be necessary to inoculate the two viruses sequentially. The currently available experimental vaccine was produced in a lyophilized state from extracts of the brains of newborn mice. Since this is a living virus vaccine comparable to that of yellow fever, very small doses are effective in producing immunity. Thus, the material extracted from the brain of a single newborn mouse can provide vaccine for 100 to 1000 men with enough to spare for an adequate margin of safety. Recent studies by Dr. Sweet and the author have shown that both immunologic types of dengue virus can multiply in monkey kidney tissue cultures without producing any cytopathogenic effect. Experiments which are now in progress should show whether or not such relatively pure tissue culture fluids might provide an alternative source of virus for vaccine production.

Past military experience has shown that sandfly fever can be an important military problem in European countries bordering on the Mediterranean and Adriatic Seas, as well as in the Middle East and the Near East, and in India where the vector Phlebotomus papatasi is present. There is reason to believe, however, that this infection is probably endemic in many other regions between 20° and 45° north latitude, from the Mediterranean all the way across Asia to the China Sea, wherever Phlebotomus papatasi may be present. At the end of World War II, there were three strains of sandfly fever virus. The one recovered from the Middle East near the Red Sea and the one recovered from Sicily were immunologically identical and produced complete cross-immunity in human beings. Another strain of virus which was recovered from an American soldier in Naples and which has since been called the Naples virus possessed the properties of the other sandfly fever strains but was immunologically completely different. At the end of World War II, experiments with these viruses could be carried out only in human beings; no experimental laboratory animal was available. In the last two years, Dr. Sweet and the author have succeeded in adapting both the Sicilian and Naples viruses to newborn mice. This has provided new tools for working with these viruses in the laboratory and also for specific diagnosis and serologic survey. Doctors R. Taylor and J. Casals, working with viruses recovered from the blood of Egyptian children, have now found at least two agents which are immunologically identical with the Sicilian strain of virus. The mouse-adapted Sicilian strain has yielded a mutant which has lost its capacity to produce the febrile systemic illness in human beings but has retained its capacity to produce immunity against the unmodified



human virus. Tests are currently in progress in human beings with the Naples mouse-adapted virus. (These tests have shown that the mouse-adapted Naples virus also lost its capacity to produce illness in human beings and can immunize against the unmodified human virus.) Such mutant strains would, of course, also be useful for artificial immunization under special circumstances. The special habits of the vector, Phlebotomus papatasi, and its remarkable susceptibility to DDT provide a means for controlling the infection in houses and tents, but, without complete elimination of the vector from an area, there would still remain considerable risk of infection to those who would have to remain in the open during the hours between sundown and sunrise.

The second category, in order of military importance, comprises those insect-borne virus infections which produce clinically manifest disease in only small numbers but which are associated with a high case fatality rate. Among these, one must mention especially the viruses of Japanese B encephalitis and the related Murray Valley encephalitis, and the Russian Spring-Summer encephalitis and its related Central European encephalitis, as well as the encephalitis viruses of the Western Hemisphere. Because of ignorance of its natural history and behavior, Japanese B encephalitis loomed as a potentially important military problem in 1945 when approximately 225,000 men were on Okinawa at a time when a few cases of the disease were first recognized on the island. Actually, although a larger number were suspected of having the disease, only 11 cases of encephalitis were finally proved to have been caused by this virus. The subsequent experience on Okinawa and in Japan, Korea, and other parts of the Far East showed that a varying and unpredictable number of cases of this disease could be expected every year. Since 1951, there have been 17 deaths from Japanese B encephalitis among American military personnel and their dependents in Japan, Okinawa, and Korea. How many of these might have been prevented if the best available vaccine had been used is difficult to estimate. In 1945, a formalinized mouse brain vaccine was prepared which, when administered in proper doses, could produce antibody in at least 50% of individuals. During 1945 and 1946, this vaccine was administered to approximately 300,000 troops, but, for various practical considerations, a vaccine of lesser potency prepared from chick embryos was then substituted. After the experience in Korea in 1950, when a considerable number of cases of Japanese B encephalitis occurred among troops who were vaccinated in various ways, some adequately and some inadequately, the whole program of vaccination against this disease was discontinued. The decision of using a vaccine of borderline efficiency against a disease of very low incidence is not an easy one. It may, perhaps, be worth noting that during the past year the author has found that the Japanese B encephalitis virus multiplies to high levels in monkey kidney tissue cultures without producing any cytopathogenic effect. It may be desirable to pursue this further to determine whether or not a vaccine prepared from this more desirable source of virus might prove to be more effective. The

recent studies on the virus recovered from Murray Valley encephalitis in Australia indicate that it is very closely related to the virus of Japanese B encephalitis. The author's interpretation of various reported and unreported studies would be that it represents a related but distinct immunologic type of the Japanese B virus. If this interpretation is correct, it becomes necessary to determine whether or not similar quantitative antigenic differences may exist among different strains of Japanese B encephalitis virus which occur in Japan, Korea, Okinawa, and other parts of the Far East outside of Australia. Unless one can show that different strains are immunologically identical, the use of a vaccine of borderline effectiveness, prepared with a single strain, could hardly be expected to provide complete protection.

The recent extensive, and as yet unpublished, work of the virus, epidemiology, and entomology divisions of the 406th General Medical Laboratory in Japan has added a great deal to the knowledge of the role of various mosquitoes and birds in the epidemiology of Japanese B encephalitis in Japan. Thus, it is quite clear now that Culex tritaeniorhynchus is the only mosquito vector in nature and that black-crowned night herons and egrets attract this mosquito and are infected by the virus. It still is not clear why no virus can be found in Culex pipiens which are also attracted in large numbers to these birds, nor has it been established whether the mosquitoes merely transmit the infection to the birds or also acquire it from them. These particular birds occur only in limited areas of Japan while infection of human beings and domestic animals is extensive throughout Japan, south of Hokkaido. Where the C. tritaeniorhynchus mosquitoes get their virus to start an epidemic is still as much of a mystery as ever. It does appear, however, that large number of these mosquitoes become infected within a few weeks prior to the appearance of an epidemic and by the time an epidemic is recognized, the vast majority of human beings have already been infected and most of the C. tritaeniorhynchus mosquitoes are either dead or uninfected. It is for these reasons that one can expect very little from heroic mosquito control measures after an epidemic has been recognized.

The basic problem of the ultimate reservoir of the St. Louis, Western equine and Eastern equine encephalitis viruses also requires elucidation and solution. Dr. Hammon informed the author that recent work in his laboratory by Dr. Preston Holden indicates that the Eastern virus has a cycle in pheasants without any arthropod vector. The high incidence of febrile illnesses without encephalitis among laboratory personnel engaged in work on Venezuelan equine encephalitis makes it highly desirable to determine whether this virus may be the cause of such unrecognized febrile diseases of man in areas where this virus is endemic, but no work on this subject has as yet been reported. The greatest progress in recent years has been made in the elucidation of the epidemiology of West Nile fever. The great



influx of immigrants to Israel, together with a group of alert investigators, brought forth unequivocal evidence that epidemics of a disease, which is clinically indistinguishable from dengue, can be caused by the mosquito-borne West Nile virus. This virus, which was first recovered in 1940 by Smithburn and his associates from the blood of a mildly ill native woman in Uganda, and subsequently from the blood of Egyptian children by Doctors Paul and Melnick, is now known to be a common cause of infection among human beings in the Nile Valley from the Southern Sudan to the Nile Delta. The experimental use of mouse-adapted strains of this virus as a possible therapeutic agent in cancer patients by Doctors Southam and Moore revealed that it can also cause encephalitis. Work at the Naval Medical Research Unit No. 3, Cairo, Egypt, aided by the Rockefeller Foundation, has contributed significantly to the epidemiology and the natural history of this infection (West Nile). According to a personal communication from Dr. Taylor, the picture is probably somewhat as follows: Transmission occurs mainly during the summer months by Culex mosquitoes and particularly Culex univittatus. The main vertebrate reservoir appears to be in birds as the virus has been isolated from both crows and pigeons, and experimentally these birds, as well as others, can be infected by mosquitoes and, in turn, transmit the infection to mosquitoes permitted to feed upon them. The infection of man, as well as other mammalian hosts, is likely secondary to the bird-mosquito cycle. The manner of over-wintering of the virus has not been definitely determined, but a virus having similar characteristics, though, perhaps, not identical to West Nile, has been isolated repeatedly from Argas ticks.

While the epidemiology of Russian Spring-Summer encephalitis in the Far East has been clearly shown by Russian investigators to be dependent on the wood tick, Ixodes persulcatus, it is not yet clear whether the recently recognized Central European encephalitis is similarly transmitted. The viruses recovered from the European disease appear to be such close antigenic variants of those found in the Far East and those associated with the tick-borne louping-ill of Northern England and Scotland, that the mode of transmission is also likely to be similar. The case fatality rate is very high and the Russians have used a formalinized mouse brain vaccine for military and other personnel operating in endemic areas, and a similar vaccine has been used to protect laboratory personnel working with this virus at the Army Medical School in Washington.

Among the other recent advances in the field of insect-borne virus diseases may, perhaps, be mentioned the development of simple and rapid diagnostic tests which are based on hemagglutination-inhibition. Because the hemagglutination-inhibition antibodies develop earlier than the complement-fixing antibodies, it is now possible to provide the clinician with a specific diagnosis by the time the temperature has returned to normal rather than weeks after the patient has died or been discharged from the

hospital. Extensive tests by Major Buescher and Captain Chanock at the 406th General Medical Laboratory in Tokyo have shown that this rapid in vitro technic is the diagnostic test of choice for Japanese B encephalitis. Adequately investigated hemagglutinins are also available for the St. Louis, West Nile, dengue and yellow fever viruses as well as the the Western and Eastern equine encephalitis viruses and some of the lesser known South American and African viruses.

The medical officer responsible for military preventive medicine wants to have answers to the following questions about the insect-borne virus diseases of man:

- 1 Which ones are endemic in certain regions?
- 2 Are they diseases of high incidence or low incidence?
- 3 What are the simplest and most rapid specific diagnostic tests?
- 4 What can be done to prevent them?

It is hoped that this discussion of recent advances and of the limitations of present knowledge has contributed at least a partial answer to these questions.

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